

REMARKS

Claims 24, 26-27, 29 and 37 were pending in the application. New claims 38 and 39 have been added, support for which can be found, for example, in [0055] and [0100] of the application as filed. Claims 24, 26, 27, and 29 have been amended to further clarify the claim language. Claim 37 was amended to recite that the polypeptide encoded by the 98% homology of SEQ ID NO:167 has the same activity as EGR1. Support for this amendment can be found, for example, in Table 1 of the application which recites that SEQ ID NO:167 is an EGR1 sequence.

No new matter has been added.

Upon entry of this amendment, claims 24, 26, 27, 29, and 37-39 will be pending.

Objections

Claims 24 and 37 were objected to due to alleged typographical errors. Applicants have amended claim 24, rendering the objection moot to the extent it applies to claim 24.

Claim 37 is alleged to contain a word which "seems out of place". Although Applicants disagree, claim 37 has been amended thereby updating the language referred to by the Office.

Rejections under 35 U.S.C. § 112, first paragraph (written description; new matter)

Claims 24, 26, 27, 29 and 37 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Although acknowledging that the claimed sequence is disclosed in the specification to be a "cancer associated (CA) nucleic acid" and that CA nucleic acids can be up or down regulated in carcinomas, the Office asserts that the specification does not disclose which CA nucleic acids are upregulated and which are downregulated." The Office further alleges that the function of the encoded Egr1 polypeptide (binding to the promoter of the inosine-5' monophosphate dehydrogenase type II gene) is not disclosed in the specification. Further, the Office asserts that "the specification provides no guidance as to what kind of proliferation activity a polypeptide encoded by SEQ ID

NO:167 would have.” As the full scope of the pending claims is supported by the present application, Applicants do not agree.

Preliminarily Applicants note that the claims have been amended, revising the language indicating the function of the encoded polypeptide, rendering the rejection moot to the extent it refers to the function of the encoded polypeptide. With respect to claim 37, although Applicants do not agree with the rejection, claim 37 has been amended and recites a function supported by the application (see, for example, Table 1).

As set forth in the MPEP, “[w]hile there is no *in haec verba* requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure.” Additionally, what is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. See *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384.

The specification as originally filed provides adequate support for the pending claims, as amended. Written description requires only that a person of ordinary skill be able to recognize that Applicants had possession of the claimed invention. Explicit support for each of the claim limitations is set forth in the specification as originally filed. Applicants note that the application is generally directed to “sequences for use in diagnosis and treatment of carcinomas.” Although colon cancer is specifically identified in the application as a cancer relevant to the claimed methods, the Office is also reminded that colon cancer is a carcinoma. The application describes the correlation of the disclosed sequences with cancer, noting that the relevant sequences are “carcinoma associated (CA)”.

To demonstrate further the written description support for the pending claims, Applicants note examples of the support for each element of claim 24; claims 26, 27, 29 and 37 are similarly supported. Applicants note that originally filed claim 11 provides support for the pending claims.

24. (as amended herein) A method of diagnosing colon cancer comprising:

a) determining the level of a nucleic acid comprising a sequence at least 98% identical to SEQ ID NO:167, or a full complement thereof, in a patient sample comprising colon tissue; and

b) comparing the level of the nucleic acid in (a) to a level of the nucleic acid in a second sample, said second sample comprising non-cancerous colon tissue;

wherein a patient sample with a level of expression of the nucleotide sequence at least 50% less than the level of expression of the nucleotide sequence in the second sample indicates that the patient has colon cancer.

Claim limitation	Exemplary support in specification
A method of diagnosing colon cancer [comprising:]	[0002] The present invention relates to novel sequences for use in <i>diagnosis</i> and treatment of <i>cancer</i> , especially <i>carcinomas</i> , as well as the use of the novel compositions in screening methods; [0021] Cancers classified by site include cancer of the oral cavity and pharynx (lip, tongue, salivary gland, floor of mouth, gum and other mouth, nasopharynx, tonsil, oropharynx, hypopharynx, other oropharynx); cancers of the digestive system (esophagus; stomach; small intestine; <i>colon</i> and rectum; ... [0134] The CA proteins, antibodies, nucleic acids, modified proteins and cells containing CA sequences are used in diagnostic assays.
[a)] determining the level of a nucleic acid comprising a sequence at least 98% identical to SEQ ID NO:167, or a full complement thereof in a patient	[0020] Accordingly, the present invention provides nucleic acid and protein sequences that are associated with carcinoma, herein termed "carcinoma associated" or "CA" sequences; [0024]

sample	<p>Association in this context means that the nucleotide or protein sequences are either differentially expressed, activated, inactivated or altered in carcinomas as compared to normal tissue; [0047] An CA sequence is initially identified by <i>substantial nucleic acid and/or amino acid sequence homology</i> to the CA sequences outlined herein. Such homology can be based upon the overall nucleic acid or amino acid sequence, and is generally determined as outlined below, using either homology programs or hybridization conditions. [0048] As used herein, a nucleic acid is a "CA nucleic acid" if the overall homology of the nucleic acid sequence to one of the nucleic acids of Table 1A-HHH is preferably greater than about 75%, more preferably greater than about 80%, even more preferably greater than about 85% and most preferably greater than 90%. In some embodiments the homology will be as high as about 93 to 95 or 98%. In a preferred embodiment, the sequences which are used to determine sequence identity or similarity are selected from those of the nucleic acids of Table 1A-HHH. [0108] CA proteins may also be identified as being encoded by CA nucleic acids. Thus, CA proteins are encoded by nucleic acids that will hybridize to the sequences of the sequence listings, <i>or their complements</i>, as outlined herein; [0118] The present invention is</p>
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	<p>directed to a number of sequences associated with carcinomas ... [0127] In one aspect, the expression levels of genes are determined for different cellular states in the carcinoma phenotype; that is, the expression levels of genes in normal tissue and in carcinoma tissue (and in some cases, for varying severities of lymphoma that relate to prognosis, as outlined below) are evaluated to provide expression profiles. [0133] In a preferred embodiment nucleic acids encoding the CA protein are detected. Although DNA or RNA encoding the CA protein may be detected, of particular interest are methods wherein the mRNA encoding a CA protein is detected. [0225] The CA nucleic acid sequences of the invention are depicted in Table 1A-HHH; Table 1 – lists cancer associated sequences</p>
comprising colon tissue [; and]	<p>[0021] <i>Cancers</i> classified by site include cancer of the oral cavity and pharynx (lip, tongue, salivary gland, floor of mouth, gum and other mouth, nasopharynx, tonsil, oropharynx, hypopharynx, other orallpharynx); cancers of the digestive system (esophagus; stomach; small intestine; <i>colon</i> and rectum; ... ; [0024] <i>Association in this context means</i> that the nucleotide or protein sequences are either <i>differentially expressed</i>, activated, inactivated or altered <i>in carcinomas as compared to normal tissue</i>. [0034] In a preferred</p>

	embodiment, CA sequences are those that are <i>down-regulated in carcinomas</i> ; that is, the <i>expression of these genes is lower in carcinoma tissue as compared to normal tissue</i> of the same differentiation stage.
b) comparing the level of the nucleic acid in (a) to a level of the nucleic acid in a second sample, said second sample comprising non-cancerous colon tissue;	[0034] that is, the expression of these genes is lower in carcinoma tissue as compared to normal tissue of the same differentiation stage. [0127] By comparing expression profiles of cells in different states, information regarding which genes are important (including both up- and down-regulation of genes) in each of these states is obtained. Then, diagnosis may be done or confirmed: does tissue from a particular patient have the gene expression profile of normal or carcinoma tissue; [0140] It is understood that when comparing the expression fingerprints between an individual and a standard, the skilled artisan can make a diagnosis as well as a prognosis.
wherein a patient sample with a level of expression of the nucleotide sequence at least 50% less than the level of expression of the nucleotide sequence in the second sample indicates that the patient has colon cancer.	[0034] <i>"Downregulation" as used herein means at least about 50%</i> , more preferably at least about 100%, more preferably at least about 150%, more preferably, at least about 200%, with from 300 to at least 1000% being especially preferred; [0192] Positive controls and negative controls may be used in the assays. [0127] By comparing expression profiles of cells in different states, information

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	regarding which genes are important (including both up- and down-regulation of genes) in each of these states is obtained. Then, diagnosis may be done or confirmed: does tissue from a particular patient have the gene expression profile of normal or carcinoma tissue;
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As set forth above, adequate support for the claimed invention is provided by the application as originally filed. Claim limitations are, at the very least supported by implicit or inherent support, more prevalently, however, by express support. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

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Conclusion

It is believed that any pending objections and rejections have been addressed. However, the absence of a reply to a specific rejection, issue, or comment does not signify agreement with or concession of that rejection, issue, or comment. In addition, because the arguments made above may not be exhaustive, there may be reasons for patentability of any or all pending claims (or other claims) that have not been expressed. Finally, nothing in this paper should be construed as an intent to concede any issue with regard to any claim, except as specifically stated in this paper, and the amendment of any claim does not necessarily signify concession of unpatentability of the claim prior to its amendment.

The examination of the pending claims and passage to allowance are respectfully requested. An early Notice of Allowance is therefore earnestly solicited. Applicant invites the Examiner to contact the undersigned at (302) 778-8458 to clarify any unresolved issues raised by this response.

Please apply any charges or credits to Deposit Account 06-1050.

Respectfully submitted,



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